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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,914	09/08/2006	Matthew M. Morrisette	21548YP	1688
210	7590	04/20/2009	EXAMINER	
MERCK AND CO., INC			SZNAIDMAN, MARCOS L	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/591,914	<b>Applicant(s)</b> MORRISSETTE ET AL.	
	<b>Examiner</b> MARCOS SZNAIDMAN	<b>Art Unit</b> 1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 13 February 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1,6,9-12,14 and 19 is/are pending in the application.
- 4a) Of the above claim(s) 14 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 11 is/are allowed.
- 6) ☒ Claim(s) 1,6,9,12 and 19 is/are rejected.
- 7) ☒ Claim(s) 10 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>4 pages / 02/13/09 and 02/16/09</u> . | 6) <input type="checkbox"/> Other: _____  |



## **DETAILED ACTION**

This office action is in response to applicant's reply filed on February 13, 2009.

### ***Status of Claims***

Amendment of claims 1, 6, 9-11 and 10, and cancellation of claims 2-5, 7-8 and 13 is acknowledged.

Claims 1, 6, 9-12, 14 and 19 are currently pending and are the subject of this office action.

Claim 14 was withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on June 28, 2008.

Claims 1, 6, 9-12, and 19 are presently under examination.

### ***Priority***

The present application is a 371 of PCT/US2005/007106 filed on 03/04/2005, and claims priority to provisional application No. 60/551,440 filed on 03/09/04.

### ***Rejections and/or Objections and Response to Arguments***

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated

(Maintained Rejections and/or Objections) or newly applied (New Rejections and/or Objections, Necessitated by Amendment or New Rejections and/or Objections not Necessitated by Amendment). They constitute the complete set presently being applied to the instant application.

***Claim Rejections - 35 USC § 112 (New Rejection not necessitated by Amendment)***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6, 9, 12, and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 1, 6, 9, 12, and 19 recite a compound represented by Formula I (see claim 1) or a pharmaceutical composition comprising a compound of Formula I wherein (see claim 1) R9 is C1-6 alkyl substituted with CycA, AryA or HetC, and wherein each HetC is independently a 4- to 7-membered saturated or unsaturated heterocyclic ring containing at least one carbon atom and from 1 to 4 heteroatoms independently selected from N, O and S; and in claim 9 R8 contains HetE and/or HetF.

M.P.E.P. #2163 states: "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention....one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process".

A description of a chemical genus will usually comprise a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the members of the genus, which features constitute substantial portion of the genus. See *Univ. of California vs. Eli Lilly*, 43 USPQ 2d 1398, 1406 (Fed. Cir. 1997). This is analogous to enablement of a genus under section 112 first, by showing enablement of a representative number of species within the genus. A chemical genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. If the genus has a substantial variance, the disclosure must describe a sufficient number of species to reflect the variation within that genus.

Applicant has failed to show that he was in possession of all the compounds encompassed by Formula I in which HetC can be a heterocycle as described above. Applicant discloses the structures of 18 compounds (see examples 1-18 on the specification) all of which show a very narrow set of substituents for R9. For example, in all the examples R9 is either: Hydrogen, methyl, or cyclopropyl. There are no

examples of R9 with an heterocycle as a substituent. This small set of compounds can not be viewed as being reasonably representative of the genus in its claimed scope because no readily apparent combination of identifying characteristics is provided, other than the disclosure of those specific species as examples of the claimed genus.

Given the broad scope of the claimed subject matter, Applicant has not provided sufficient written description that would allow the skilled in the art to recognize all the compounds of formula I claimed.

In order to bring the claims in compliance with what is disclosed, it is suggested that applicant provides a more specific and narrower definition of the term HetC in claim 1 and HetE and HetF in claim 9 more consistent to what is disclosed in the specification.

Claims 1, 6, 9, 12, and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds listed in claims 10 and 11, does not reasonably provide enablement for the remaining compounds claimed in formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. This is a scope of enablement rejection.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fd. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. *PPG v. Guardian*, 75 F.3d 1558, 1564 (Fed. Cir. 1996). As pointed out by the court in *In re Angstadt*, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) at 547 the court recited eight factors:

- 1- the quantity of experimentation necessary,
- 2- the amount of direction or guidance provided,
- 3- the presence or absence of working examples,
- 4- the nature of the invention,
- 5- the state of the prior art,
- 6- the relative skill of those in the art,
- 7- the predictability of the art, and
- 8- the breadth of the claims

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping



that in mind, the *Wands* factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention

Claims 1, 6, 9, 12, and 19 recite a compound represented by formula I (see claim 1) or a pharmaceutical composition comprising a compound of formula I.

2. The relative skill of those in the art

The relative skill of those in the art is high, generally that of an M.D. or Ph.D. The artisan using Applicant's invention would generally be a physician with a M.D. degree and several years of experience.

3. The state and predictability of the art

Since the compounds of claim 1 are novel there is no synthetic procedure for these particular compounds in the prior art.

It is well known in the prior art that organic synthesis is still an experimental science. Even though the knowledge of organic synthesis and the arsenal of chemical reactions have exploded in the last decades, there is still a high degree of unpredictability in organic synthesis. See for example Dorwald F. A. (Side reactions in organic synthesis, 2005, Wiley, VCH, Weinheim, pg. IX of Preface) where it says: "Most non-chemists would probably be horrified if they were to learn how many attempted synthesis fail, and how inefficient research chemists are. The ratio of successful to

unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working on what went wrong, and why. He later states: "The final synthesis usually looks like quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even repetition) of a synthesis usually implies will be able to appraise such work". And finally: "Chemists tend not to publish negative results, because these are, as opposed to positive results, never definitive (and far too copious)."

4. The breadth of the claims

Claims 1, 6, 9, 12, and 19 are very broad in terms of the number of compounds claimed, since HetC in claim 1, and HetE and HetF in claim 9 are very broad.

5. The amount of direction or guidance provided and the presence or absence of working examples

Applicant provides general synthetic schemes (see schemes 1 through 9) for some of these compounds. However, even though applicant claims an extensive and diverse set of substituents for R8 and R9 (see claim 1); the actual compounds disclosed (18 total, see examples 1 through 18) show a very narrow and defined set of R8 (HetE and HetF) and R9 (HetC) substituents.

6. The quantity of experimentation necessary

As discussed above (see: 3. the state and predictability of the art), small changes in the structure of one of the reagents could cause a completely different synthetic outcome (i.e. different products, lower yields or no reaction at all). Based on this, and since applicant claims such a diverse set of heterocyclic compounds for HetC, HetE and HetF (see: 5. The amount of direction or guidance and the presence or absence of working examples above) it is expected that some, if not most of the HetC, HetE or HetF substituents recited in claims 1 and 9 (except for those specifically listed in claims 10 and 11) will not provide the desired synthetic outcome outlined by applicant in schemes 1 through 9.

So, determining how to make a particular compound with an HetC, HetE or HetF etc. group not included in claims 10 and 11 would require testing of new synthetic pathways for the different compounds. This is undue experimentation given the limited guidance and direction provided by Applicants.

Accordingly, the inventions of claims 1, 6, 9, 12, and 19 do not comply with the scope of enablement requirement of 35 U.S.C 112, first paragraph, since to practice the claimed invention a person of ordinary skill in the art would have to engage in undue experimentation with no reasonable expectation of success.

***Allowable Subject Matter***

Claim 11 is allowed.

***Claim Objections***

Claim 10 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Conclusion***

Claims 1, 6, 9, 12, and 19 are rejected.

Claim 10 is objected.

Claim 11 is allowed.

***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571 272-0580. The fax phone

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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/  
Examiner, Art Unit 1612  
April 16, 2009.

/Brandon J Fetterolf/  
Primary Examiner, Art Unit 1642